09/682,769

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=> s phosphatidylserine(10a)memor###
L1          62 PHOSPHATIDYLSERINE(10A) MEMOR###

=> s l1 and ag###
L2          45 L1 AND AG###

=> s phosphatidylserine(10a)memory(10a)aging
L3          10 PHOSPHATIDYLSERINE(10A) MEMORY(10A) AGING

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           10 DUP REM L3 (0 DUPLICATES REMOVED)

=> d l4 bib ab kwic

L4   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2003 ACS
AN   2002:777613  CAPLUS
DN   137:262213
TI   Carbohydrate-high phosphatidylserine-containing food item for increasing
     cognitive capacity
IN   Geiss, Kurt-Reiner
PA   Giventis G.m.b.H., Germany
SO   PCT Int. Appl., 18 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
```

Dianov et al. disclose that the extent and location of DNA repair synthesis in a double stranded oligonucleotide containing a single dUMP residue have been determined in which the repair pathway of a dUMP residue in DNA involves uracil- DNA glycosylase and incision of the phosphodiester bond 5' to AP site by an AP endonuclease and baseless sugar-phosphate residue could be excised by a dRpase or a 5'-3'exonuclease to leave a hydroxy group at the 3' terminus (See pg. 1606, fig, 1) (as recited in claims 3-6) and then the polymerase step occur either after of before the excision step. The excision step is catalyzed usually by a DNA deoxyribophosphodiesterase (See pg. 1605, the Abstract) (as recited in claim 7).

One of ordinary skill in the art at the time of instant invention would have been motivated to combine the teachings of McCarthy et al., Chirikjian et al. and Dianov et al. to characterize nucleic acid molecules because the method of McCarthy et al. is used to detect multiple known mutations in DNA which can be achieved rapidly and easily (See pg. 8, lines 23-27), the method of Chirikjian et al. is efficient and sensitive by using the probe (See column 8, lines 47-50) with labeled nucleotides for the signal (See column 2, lines 48 and column 8, lines 47-49), and the teachings of Dianov et al. indicate that the enzyme used in excision repair involving AP sites is good candidates to carry out each step in the pathway (See pg. 16, column 1, last paragraph). Thus, it would have been prima facie obvious to carry out the method of characterizing DNA molecule with combining the teachings of McCarthy et al., Chirikjian et al. and Dianov et al.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002078464	A2	20021010	WO 2002-EP2694	20020312
	WO 2002078464	A3	20021205		

W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI AT 2001-482 A 20010326

AB The invention relates to a food item, preferably a bar of chocolate, that has a phosphatidylserine content of 100 mg to 300 mg and a relatively high carbohydrate content. The combination of phosphatidylserine and carbohydrates allows for both a short-term and a long-term increase in cognitive capacity in individuals over the age of around 40, esp. when the food item is consumed regularly.

ST health food carbohydrate **phosphatidylserine** cognition **memory** learning **aging**

=> d l4 2-10 bib ab kwic

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 2001:607230 CAPLUS

DN 136:101683

TI The influence of soy-derived phosphatidylserine on cognition in age-associated memory impairment

AU Jorissen, B. L.; Brouns, F.; Van Boxtel, M. P. J.; Ponds, R. W. H. M.; Verhey, F. R. J.; Jolles, J.; Riedel, W. J.

CS Experimental Psychopharmacology Unit, Brain & Behaviour Institute, Department of Psychiatry and Neuropsychology, Universiteit Maastricht, Maastricht, 6200 MD, Neth.

SO Nutritional Neuroscience (2001), 4(2), 121-134
CODEN: NNINFE; ISSN: 1028-415X

PB Harwood Academic Publishers

DT Journal

LA English

AB Phosphatidylserine (PS) is a phospholipid widely sold as a nutritional supplement. PS has been claimed to enhance neuronal membrane function and hence cognitive function, esp. in the elderly. We report the results of a clin. trial of soybean-derived PS (S-PS) in aging subjects with memory complaints. Subjects were 120 elderly (>57 yr) of both sexes who fulfilled the more stringent criteria for age-assocd. memory impairment (AAMI); some also fulfilled the criteria for age-assocd. cognitive decline. Subjects were allocated at random to one of the 3 treatment groups: placebo, 300 mg S-PS daily, or 600 mg S-PS daily. Assessments were carried out at baseline, after 6 and 12 wk of treatment; and after a wash-out period of 3 wk. Tests of learning and memory, choice reaction time, planning and attentional functions were administered at each assessment. Delayed recall and recognition of a previously learned word list comprised the primary outcome measures. No significant differences were found in any of the outcome variables between the treatment groups. There were also no significant interactions between treatment and "severity of memory complaints". In conclusion, a daily supplement of S-PS does not affect memory or other cognitive functions in older individuals with memory complaints.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Aging**, animal
(elderly; influence of soy-derived **phosphatidylserine** on

ssDNA and the new strand is synthesized in vitro with DNA polymerase and ligase (See column 4, lines 7-12).

One of ordinary skill in the art at the time of instant invention would have been motivated to combine the teachings of McCarthy et al. and Chirikjian et al. to characterize nucleic acid molecules because the method of McCarthy et al. is used to detect multiple known mutations in DNA which can be achieved rapidly and easily (See pg. 8, lines 23-27) and the method of Chirikjian et al. is efficient and sensitive by using the probe (See column 8, lines 47-50) with labeled nucleotides for the signal (See column 2, lines 48 and column 8, lines 47-49). Thus, an ordinary skill in the art would have involved the probe as taught by Chirikjian et al. for characterizing nucleic acid. Thus, it would have been prima facie obvious to carry out the method as claimed.

4. Claims 3-7 remain rejected under 35 U.S.C.§ 103(a) over McCarthy et al. (WO 97/03210) in view of Chirikjian et al. (5,656,430) as applied to claims 1-2 and 8-23 above, and further in view of Dianov et al. (Molecular and Cellular Biology, 1992, Vol. 12(4), pg. 1605-1612).

The teachings of McCarthy et al. and Chirikjian et al. are set forth in section 3 above and the methods of McCarthy et al. and Chirikjian et al. do not involving using 5' AP endonuclease and a 5' deoxyribophosphodiesterase as claimed in claims 3-7) to treat the apurinic and apyridimic sites (See pg. 23, lines 9-15).

cognition in age-assocd. **memory** impairment)

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 2000:86452 CAPLUS
DN 133:30052
TI Phosphatidylserine and memory problems in aged subjects
AU Louis-Sylvestre, Jeanine
CS Laboratoire de Physiologie du Comportement Alimentaire, EPHE, Faculte Leonard de Vinci, Bobigny, 93017, Fr.
SO Cahiers de Nutrition et de Dietetique (1999), 34(6), 349-357
CODEN: CNDQA8; ISSN: 0007-9960
PB Masson Editeur
DT Journal; General Review
LA French
AB A review with 47 refs. Because of the const. increase in life expectancy in humans, it is important to prevent or delay age-related memory and cognitive deficits. Phosphatidylserine (PS) forms 10-20% of the bilayer portion of the cell membrane. The daily dietary PS intakes are .apprx.80 mg and 300 mg oral supplements are used in most clin. studies. These studies show an efficacy of PS in subjects with age-related memory impairment and Alzheimer disease. PS partially mends modifications of the brain membrane structure related to age and has no effect in young subjects. Pharmacol. studies in animals show that PS influences membrane compn., cell metab., and interneuronal communications. Initially extd. from the bovine cerebral cortex, PS is now synthesized from soybean phosphatidylcholines. Studies show that PS efficacy does not depend on PS sources.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
ST review nutrition **phosphatidylserine memory** deficit prevention **aging**
IT **Aging**, animal
(elderly; dietary **phosphatidylserine** and **memory** deficits prevention in aged humans)

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1993:671 CAPLUS
DN 118:671
TI Behavioral and morpho-functional correlates of brain aging: a preclinical study with phosphatidylserine
AU Nunzi, Maria Grazia; Guidolin, Diego; Petrelli, Lucia; Polato, Patrizia; Zanotti, Adriano
CS Fidia Res. Lab., Abano Terme, 35031, Italy
SO Advances in Experimental Medicine and Biology (1992), 318(Neurobiol. Essent. Fatty Acids), 393-8
CODEN: AEMBAP; ISSN: 0065-2598
DT Journal
LA English
AB Degeneration of basal forebrain cholinergic neurons and loss of synapses correlate with cognitive changes during aging in both rats and man, suggesting a common pathol. process in both species. Long-term oral PS administration restores biochem. properties of cholinergic neurons in the septo-hippocampal system, enhances hippocampal synaptic plasticity and improves cognitive functions in aged memory-deficient rats. Since PS treatment prevents or improves biol. and behavioral deficits inherent to the aging process in exptl. animals, this phospholipid may find application as a therapeutic agent for age-assocd. memory dysfunctions.
ST **aging memory** brain neurotransmission **phosphatidylserine**
IT **Memory**, biological
(**aging** effect on, **phosphatidylserine** administration modulation of)

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS

nucleotide (See pg. 9, lines 5-6) (as recited in claims 10-12, 14, 15,16). The method is used for detecting multiple known mutation in DNA (See pg. 8, lines 23-27) (as recited in claim 21 and 23). The amplification method involves ligase chain reaction and deoxyribonucleotide (See pg. 9, lines 11-18) (as recited in claim 13, and 17). A modified nucleotide can be incorporated into a nucleic acid during amplification (See pg. 9, lines 18-20) (as recited in claim 8). One primer is labeled when an amplification method is used in the invention to allow detection of amplified target or complementary strand alone (See pg. 12, lines 7-10). The detection is done by using appropriate nucleic acid hybridization probe (See pg. 12, lines 22-25) (as recited in claim 20). This suggests that there must be a reporter oligonucleotide for the hybridization probe (as recited in 18). To facilitates detection of the cleaved extended adjacent primer, the extended adjacent primer denatured by denaturating polyacrylamide gel electrophoresis (See pg. 17, lines 9-18) (as recited in claim 9 that the amplified strands are separated for a separate analysis of the respective strands).

McCarthy et al. do not disclose that an upstream fragment formed as claimed is extended with a template and the extendible upstream fragment is incubated with ligase in the presence of a reporter oligonucleotide as recited in claim 18.

Chirikjian et al. disclose a method for detecting point mutation in nucleic acid sequence in which 5' probe cleaved and binds to a template for DNA polymerase with dNTP (See column 8, lines 47-50) and a probe is hybridized to single stranded DNA generating a mismatch in the

AN 1989:609093 CAPLUS
DN 111:209093
TI Chronic phosphatidylserine treatment improves spatial memory and passive avoidance in aged rats
AU Zanotti, A.; Valzelli, L.; Toffano, G.
CS Fidia Res. Lab., Abano Terme, I-35031, Italy
SO Psychopharmacology (Berlin, Germany) (1989), 99(3), 316-21
CODEN: PSCHDL; ISSN: 0033-3158
DT Journal
LA English
AB Learning/memory deficits in senescent animals are widely used as a tool to evaluate the therapeutic potential of agents for treatment of age-assocd. cognitive dysfunction. As assessed in the Morris water maze test, aged (21-24 mo) rats showed a variable loss of spatial memory. Aged non-impaired rats performed as well as young subjects, while aged impaired rats exhibited a severe and persistent place-navigation deficit. Passive avoidance retention was similarly affected in the two aged subpopulations. Chronic oral administration of phosphatidylserine (50 mg/kg/day for up to 12 wk), a pharmacol. active phospholipid, improved both the spatial memory and the passive avoidance retention of aged impaired rats. Results are discussed with ref. to the phosphatidylserine-induced improvement of age-assocd. deterioration of brain functions in rats.
IT Learning
Memory, biological
(deficits, in **aging**, chronic **phosphatidylserine** treatment effect on)

L4 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1990:92877 BIOSIS
DN BA89:52228
TI NOOTROPIC DRUGS AND BRAIN CHOLINERGIC MECHANISMS.
AU PEPEU G; SPIGNOLI G
CS DEP. PRECLIN. CLIN. PHARMACOL., UNIV. MORGAGNI 65, 50127 FLORENCE, ITALY.
SO PROG NEURO-PSYCHOPHARMACOL BIOL PSYCHIATRY, (1989) 13 (SUPPL), S77-S88.
CODEN: PNPPD7. ISSN: 0278-5846.
FS BA; OLD
LA English
AB 1. This review has two aims: first, to marshal and discuss evidences demonstrating an interaction between nootropic drugs and brain cholinergic mechanisms; second, to define the relationship between the effects on cholinergic mechanisms and the cognitive process. 2. Direct or indirect evidences indicating an activation of cholinergic mechanisms exist for pyrrolidinone derivatives including piracetam, oxiracetam, aniracetam, pyroglutamic acid, tenilsetam and pramiracetam and for miscellaneous chemical structures such as vinpocetine, naloxone, ebiratide and phosphoatidylserine. All these drugs prevent or revert scopolamine-induced disruption of several learning and memory paradigms in animal and man. 3. Some of the pyrrolidinone derivatives also prevent amnesia associated with inhibition of acetylcholine synthesis brought about by hemicholinium. Oxiracetam prevents the decrease in brain acetylcholine and amnesia caused by electroconvulsive shock. Oxiracetam, aniracetam and pyroglutamic acid prevent brain acetylcholine decrease and amnesia induced by scopolamine. Comparable bell-shaped dose-effect relationships result for both actions. Phosphatidylserine restores acetylcholine synthesis and conditioned responses in aging rats. 4. The mechanisms through which the action on cholinergic systems might take place, including stimulation of the high affinity choline uptake, are discussed. The information available are not yet sufficient to define at which steps of the cognitive process the action on cholinergic system plays a role and which are the influences of the changes in cholinergic function on other neurochemical mechanisms of learning and memory.
IT Miscellaneous Descriptors
HUMAN RAT PIRACETAM OXIRACETAM ANIRACETAM PYROGLUTAMIC ACID TENILSETAM PRAMIRACETAM VINPOCETINE NALOXONE EBIRATIDE **PHOSPHATIDYLSERINE**

characterizing nucleic acid molecules comprising introducing a modified base which is a substrate of DNA glycosylase into a DNA molecule, excising the modified based by the DNA glycosylase, cleaving the DNA at the abasic site to generate an upstream DNA fragment that can be extended in the presence of an enzyme and a template nucleic acid and analyzing the resultant fragments. The subject of the instant invention encompasses the method of claims 1, 2, 4-7, 12-13, 15-19 of U.S. Patent No. 5,952,176 because the claims are drawn to a method for rapidly detecting the presence or absence of a particular nucleic acid sequence at a candidate locus involving the steps in instant claims 1-5, 8, 10-12, 14-16 and 20-23 except that in the instant claims an upstream DNA fragment is formed by cleaving the DNA at the abasic site and extended. This technique is taught by Chirikjian et al.. Chirikjian et al. disclose a method for detecting point mutation in nucleic acid sequence in which 5' probe cleaved and binds to a template for DNA polymerase with dNTP (See column 8, lines 47-50).

3. Claims 1-2 and 8-21, 23 remain rejected under 35 U.S.C.§ 103(a) over McCarthy et al. (WO 97/03210) in view of Chirikjian et al. (5,656,430).

McCarthy et al. disclose a method for detecting a nucleic acid sequence at a locus in a target sample nucleic acid. The method involves introducing a modified base which is a substrate for a DNA glycosylase into a DNA molecule, excising the modified base by DNA glycosylase, cleaving phosphate linkages at abasic sites and analyzing the cleaved products of step iii) to identify the target nucleic acid (See pg. 8, lines 9-22) (as recited in claim 1-2, 4). The locus is amplified using normal DNA precursor nucleotides and at least one modified precursor

AUTONOMIC-DRUG COGNITION ACTIVATOR ANTIDOTE-DRUG ACETYLCHOLINE LEARNING **MEMORY** AMNESIA SCOPOLAMINE HEMICHOLINIUM ELECTROCONVULSIVE SHOCK **AGING**

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1989:660 CAPLUS
DN 110:660
TI The therapeutic value of phosphatidylserine effect in the aging brain
AU Toffano, Gino
CS Fidia Neurobiol. Res. Lab., Abano Terme, 35031, Italy
SO Advances in Behavioral Biology (1987), 33(Lecithin), 137-46
CODEN: ADBBBW; ISSN: 0099-6246
DT Journal
LA English
AB Old and possibly new data are reported which showed that administration of phosphatidylserine (from bovine brain) to rats was capable of: (1) reversing age-dependent EEG abnormalities, (2) inhibiting age-related deficits in memory and learning, and (3) preventing the age-dependent loss of hippocampal dendritic spines.
ST brain aging phosphatidylserine; **memory aging phosphatidylserine**; learning aging phosphatidylserine
IT Learning
Memory, biological
(**aging** impairment of, **phosphatidylserine** inhibition of)

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1986:490711 CAPLUS
DN 105:90711
TI Learning and memory deficits in rats during aging: effect of posphatidylserine treatments
AU Zanotti, A.; Aporti, F.; Rubini, R.; Toffano, G.
CS Fidia Neurobiol. Res. Lab., Abano Terme, 35031, Italy
SO Symposia in Neuroscience (1986), 3(Modulation Cent. Peripher. Transm. Funct.), 323-30
CODEN: SYNEE7
DT Journal
LA English
AB Behavioral tests to evaluate learning and memory in old rats showed that chronic treatment with bovine cortical phosphatidylserine (PS) reversed the age-related decline of cognitive function and also decreased the no. of spike-wave discharges in the EEG, considered to be an electrophysiol. correlate of brain aging. Chronic treatment of young rats with the PS prepn. prevented the age-related decline of active avoidance acquisition. Also, acute PS administration partially antagonized scopolamine-induced amnesia in young rats, another model of age-related memory disturbances. PS is suggested for therapy of cognitive disturbances in elderly people.
ST **aging** learning **memory phosphatidylserine**

L4 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1986:391246 BIOSIS
DN BR31:76866
TI LEARNING AND **MEMORY** DEFICITS IN RATS DURING **AGING** EFFECT OF **PHOSPHATIDYLSERINE** TREATMENTS.
AU ZANOTTI A; APORTI F; RUBINI R; TOFFANO G
CS FIDIA NEUROBIOL. RES. LAB., VIA PONTE DELLA FABBRICA 3/A, 35031 ABANO, TERME, ITALY.
SO BIGGIO, G. ET AL. (ED.). SYMPOSIA IN NEUROSCIENCE, VOL. 3. MODULATION OF CENTRAL AND PERIPHERAL TRANSMITTER FUNCTION; 4TH CAPO BOI CONFERENCE, VILLASIMIUS, ITALY, JUNE 2-7, 1985. XII+624P. LIVIANA PRESS: PADOVA, ITALY (DIST. BY SPRINGER-VERLAG: NEW YORK, N.Y., USA; BERLIN, WEST GERMANY). ILLUS. (1986) 0 (0), 323-330.
CODEN: SYNEE7. ISBN: 88-7675-462-8, 0-387-96329-4, 3-540-96329-4.
FS BR; OLD

not involve mismatch and the glycosylase of the present invention is specific for modified bases. and excises them to form abasic sites. However, the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

The response additionally argues that the probe DNA in the teachings of Chirikjian et al. is an exogenously added DNA, while in the present invention, the extended DNA is an endogenous DNA molecule, i.e. a piece of DNA produced in the reaction as part of the claimed process. Nevertheless, the teachings of Chirikjian et al. disclose that the 5' end of the probe upon cleavage has remained bound to the target polynucleotide can form a template for DNA polymerase (See column 8, lines 47-49).Thus, it is unclear whether the DNA used in the instant invention is exogenous or endogenous DNA. It appears that the DNA in claim 1 of the instant invention can be interpreted as an exogenous DNA or endogenous DNA.

Finally, regarding the argument of the reference of Dianov et al., the teachings of Dianov et al. encompass the limitations of claims 3-7 as set forth in the Office action mailed 7/05/2001.

Based upon the discussion above, the rejections are maintained. Each reaction is restates as follows.

2. claims 1-5, 8, 10-12, 14-16 and 20-21, 23 remain rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1, 2, 4-7, 12-13 and 15-19 of McCarthy et al. U.S. Pat. No. 5,952,176 in view of Chirikjian et al. (5,656,430).

Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-5, 8, 10-12, 14-16 and 20-23 are drawn to a method of

LA English
TI LEARNING AND **MEMORY** DEFICITS IN RATS DURING **AGING** EFFECT OF **PHOSPHATIDYLSERINE** TREATMENTS.

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1988:597 CAPLUS
DN 108:597
TI Pharmacological properties of phosphatidylserine in the aging brain: biochemical aspects and therapeutic potential
AU Calderini, G.; Bellini, F.; Bonetti, A. C.; Galbiati, E.; Rubini, R.; Zanotti, A.; Toffano, G.
CS Fidia Neurobiol. Res. Lab., Abano Terme, Italy
SO FIDIA Research Series (1986), 4(Phospholipid Res. Nerv. Syst.), 233-41
CODEN: FRSEEA
DT Journal
LA English
AB **Phosphatidylserine** (I) improved **memory** function that was altered by the **aging** process; this effect of I was paralleled by a normalization of the EEG, suggesting a close relationship between the 2 events.
AB **Phosphatidylserine** (I) improved **memory** function that was altered by the **aging** process; this effect of I was paralleled by a normalization of the EEG, suggesting a close relationship between the 2 events.
IT **Memory**, biological
(impairment of, in **aging**, **phosphatidylserine** treatment of)

This Office action replies the response filed 4/02/2003.

Claims 1-21 and 23 are pending.

1. The response filed 4/2/2003 argues that the examiner's statement in the advisory action mailed 1/14/2003 is unclear and contradictory in which the examiner's first state the teachings of McCarthy et al., instead of citing to particular portion of McCarthy et al. to support the rejection, instead of that examiner cites the teachings of Dianov et al.

The reason to cite the teachings of Dianov et al. is that cleaving phosphate linkage of DNA molecule at an abasic site in which the 3' hydroxyl terminus is generated was well known in the art at the time of the instant invention as taught by Dianov et al. (See pg. 1606, fig. 1 of the reference of Dianov et al.).

Although the response argues that McCarthy et al. do not disclose that cleaving phosphate linkage of DNA molecule at an abasic site in which the 3' hydroxyl terminus is generated, this reaction generating 3' hydroxyl terminus is encompassed in the teachings of Dianov et al. (See pg. 1606, fig. 1 of the reference of Dianov et al.).

The response also argues regarding the issue that the claims do not specify which group of the DNA is cleaved and the teachings of McCarthy et al. encompasses the limitations in the claims. The examiner agrees that the claims dictate where the cleavage occurs and McCarthy et al. encompasses the limitations in the claims.

The response further argues regarding the reference of Chirikjian et al. that the glycosylase of Chirikjian et al. recognizes and cleaves mismatches, the present invention does